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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/523,102	03/10/2000	Erwin Si	03654.0255	4492

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EXAMINER	
SAUCIER, SANDRA E	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/523,102	SI ET AL.	
	Examiner	Art Unit	
	Sandra Saucier	1651	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 26 May 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): 112, second para.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See attachment*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1-42*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☒ Other: *PTO-892*

Sandra Saucier
Primary Examiner
Art Unit: 1651

Attachment to the Advisory

Applicants argue that neither WO 97/41844 nor US 5,763621 teach the treatment of retinal neovascularization by topical administration of batimastat to the eye.

Please note that US 5,767,153 teach the topical administration (column 2, line 6) of batimastat and polycarbophil to the eye, see example 6. While this reference does not have an exemplification of the generic method, it specifically teaches topical administration of a composition of batimastat, which is known to be effective to treat proliferative retinopathies (US 5,7,63,621). Inherent in this administration would be the prevention of neovascularization since all humans are in need of such prevention.

US 5,763,621 directly teaches that batimastat type compounds are effective for treating proliferative retinopathies (column 1, line 30) and teaches topical application to the eye in column 11, line 44 of 10 to 100 mg. The reference does not exemplify this generic method.

Applicants appear to argue that there is no suggestion to treat retinal neovascularization by topically administering a composition capable of delivering a therapeutically effective amount of a batimastat compound to the retina. Please note that "capable of delivering" is directed to an inherent capacity of the composition of the claims. Further, this allegation is not well taken. WO 97/41844 clearly teaches the administration of combinations of angiostatic compounds to prevent pathological neovascularization (abstract) such as diabetic retinopathy (page 1, l. 21). Batimastat is one of the specific angiostatic agents to be administered. In Example 1, a **topical** composition for controlling ocular neovascularization is taught. It appears to have two angiostatic compounds in concentration of 0.005-5% wt/wt and a polymer (tyloxapol). There appears to be a teaching of a topical administration to treat ocular neovascularization including diabetic retinopathy which is type of ocular neovascularization. It is, however, true that there is no exemplification of this method. Applicants present the reference of Geroski *et al.*, which has been

carefully reread, to urge that one of skill in the art would have no reasonable expectation that topical administration to the eye would be an effective means to accomplish delivery of a therapeutic amount of a batimastat compound to the retina. While the reference does state that drug delivery to posterior segment remains a significant challenge, topical application of drugs to treat diseases of posterior segment of the eye are known in the prior art. See WO 96/03985 [IDS] where topical administration of a drug is exemplified and posterior segments of the eye are demonstrated to respond, see examples. Also, Ricci *et al.* [abstract attached] show in an experiment similar to that in the instant specification, that oxygen-induced retinopathy (neovascularization) is treatable by topically applied timolol maleate. A significant challenge in drug delivery via topical, ocular administration may remain according to Geroski *et al.*, but the prior art clearly shows that it is possible to treat posterior segment conditions by topical application of drugs in the form of working examples and experimental results.

Applicants state that US 5,763,621 teaches away from the instant claims. Please note that omitting an exemplification of a generic teaching is not the same as a teaching away from the claims. Applicants state that '621 does not teach or suggest the use of batimastat compounds in the instantly claimed methods. This is not well taken as '621 certainly does teach a topical ocular formulation which contain batimastat angiostatic compounds. Please see the compound of formula I in column 4. Applicants' compound is encompassed by the formula. This family of compounds is disclosed as having metalloproteinase inhibition activity. MMP inhibitors are disclosed to be effective against angiogenesis dependent diseases including proliferative retinopathy (col. 1, ls. 27-30). This is surely at the very least a suggestion to topically apply the compounds of formula I to treat proliferative retinopathies. No teaching away is seen. It is acknowledged that the presentation of unexpected results would permit allowance of some of the claims which were commensurate in scope with the results.

Applicants might argue that batimastat is a water insoluble compound and that water insoluble compounds, unlike the compounds of WO 96/03985 [IDS] or Ricci *et al.* would not be expected to be effective in posterior segment eye disease because water insoluble drugs do not pass through the blood-retinal barrier. Some extrinsic evidence directed towards this element coupled with limitation to the insoluble batimastat type compounds might be persuasive of unexpected results.

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